Application No. 10/595,571 Attorney Docket No. 22727/04393 Preliminary Amendment

Amendments to the Specification:

Please delete paragraphs [030] to [035] and replace them with the following paragraphs:

[030] Fig. 1 shows the amino acid sequence for Las1 protein from human (SEQ ID NO: 1).

[031] Fig. 2 shows the nucleotide sequence which encodes the human Las1 protein (SEQ ID NO: 2).

[032] Fig. 3. shows the amino acid sequence for the mouse Las1 protein (SEQ ID NO: 3).

[033] Fig. 4 shows the nucleotide sequence which encodes the mouse Las1 protein (SEQ ID NO: 4).

[034] Fig. 5. Characterizations of the Pas1 locus. (A). Substitution mapping of Pas1 QTL for mouse lung tumor susceptibility with the use of a set of congenic strains. The open boxes represent a chromosome fragment from the donor strain (A/J), and the solid boxes represent a chromosome fragment from the recipient strains (C57BL/6J). Eight microsatellite markers were used to alleleotype the 26.1 cM region containing the Pas1 locus. AB is a congenic strain in which the entire chromosomal region between markers D6MIT54 and D6MIT373 has been substituted into the recipient C57BL6J strain from the donor A/J strain. Congenic substrains 1 through 8 carry various donor (A/J) fragments as indicated. BB is the control congenic strain in which no substitution was found in the entire region. (B) Expression of Pas1 candidate genes in mouse lungs. Total RNAs were isolated from A/J and C57BL/6J normal lung tissues. Expression levels of five candidate genes were tested using RT-PCR and Northern blot analysis.

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For each autoradiograph, Upper panel, individual candidate genes; lower panel, b-actin control. For each candidate gene, the left panel, expression level in C57BL6J lungs; the right panel, expression level in A/J lungs. Note: Bcat1, Lrmp, AK015530, AK016641 are Kras2 is Northern blot analysis. (C) Functional polymorphisms of Pas1 RT-PCR. candidate genes (SEQ ID NOS 5-20, respectively, in order or appearance). Sequence analysis of the Las1 gene revealed a functional polymorphism at codon 60 between lung tumor susceptible/intermediate (A/J, SWR/J, BALB/cJ, 129/J, CBA/J, and SM/J) (top) and resistant strains (C57BL/6J, DBA/2J, SJL/J, C3H/HeJ, AKR/J, and Mus. Spretus) (bottom). An amino acid alignment of the codon 52-72 of Las1 is shown, with the asparagine to serine alteration at codon 60 (boxed). 2. Sequence variations of Ak016641 between A/J and C57BL/6J. AK016641 contains 2 functional polymorphisms at codon 218 (Arg to His), codon 258 (Gly to Glu) and an alternative splicing transcript without exon 5 only found in A/J strain. 3. AK015530 had a polymorphism at codon 28 resulting a change of Asp to Gly. 4. Lrmp contains 5 functional polymorphisms including codon 31 (Asp to Gly), codon 56 (Gly to Asp), codon 58 (Phe to Leu), codon 438 (Arg to Glv), and codon 537 (Pro to Leu).

[035] Fig. 6. Cluster alignment of mouse (SEQ ID NO: 21) rat (SEQ ID NO: 24) human (SEQ ID NO: 22) and Ciona intestinalis (SEQ ID NO: 23) Las1 protein sequences. The sequences of mouse, rat, human, and Ciona intestinalis Las1 are presented. Identical residues are shaded in black. Residues identical in at least two species are shaded in black. In mouse protein, the codon 60 ("x") encodes an Asparagine (AAT) in A/J mice and a Serine (AGT) in C57BL/6J mice. The human protein sequence (67% identities and 81% positives) is based on predicted human Las1 cDNA sequence. Searching NCBI protein database using mouse protein sequence revealed a rat homologous protein, encoded by NCBI predicted gene LOC297720 (84% identities and 92% positives). The mouse Las1 protein is also homologous to a Ciona intestinalis protein axonemal p83.9 (GI: 20086393, 33% identities and 52% positives).

Please delete paragraphs [039] to [048] and replace them with the following paragraphs:

[039] Fig. 10 shows the nucleotide sequence for human LRMP (SEQ ID NO: 25).

[040] Fig. 11 shows the nucleotide sequence for mouse LRMP (SEQ ID NO: 26).

[041] Fig. 12 shows the human BCAT1 cDNA sequence (SEQ ID NO: 27).

[042] Fig. 13 shows the mouse BCAT1 cDNA sequence (SEQ ID NO: 28).

[043] Fig. 14 shows the human Kras2 isoform a cDNA sequence (SEQ ID NO: 29).

[044] Fig. 15 shows the human Kras2 isoform b cDNA sequence (SEQ ID NO: 30).

[045] Fig. 16 shows the mouse Kras2 isoform a cDNA sequence (SEQ ID NO: 31).

[046] Fig. 17 shows the mouse Kras2 isoform b cDNA sequence (SEQ ID NO: 32).

[047] Fig. 18 shows the mouse Ak016641 cDNA sequence (SEQ ID NO: 33).

[048] Fig. 19 shows the mouse Ak015530 cDNA sequence (SEQ ID NO: 34).

Please delete paragraphs [069] and [070] and replace them with the following paragraphs:

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[069] 5'- GACCAAAGCCGAGCGACTGCGGC (SEQ ID NO: 35);

[070] 3'-TCGAAGAAGTAGTTCTGTGGC (SEQ ID NO: 36)

Please delete paragraph [0147] and replace it with the following paragraph:

[0147] Northern Blot Analysis and Semiquantative RT-PCR. Total RNAs were prepared from mouse lung tissues using TRIzol reagent (Life Technologies). Poly(A)+ RNAs were purified from the total RNAs with MicroPoly(A)Pure (Ambion). A 2-microgram aliquot of each Poly(A)+ RNA was separated on a 1% agarose gel containing 2% formaldehyde and transferred to nylon membrane. The blots were hybridized with a random-primed 32P-labelled cDNA probe in ExpressHybTM Hybridization Solution (Clontech) at 68 °C, washed with 0.1XSSC-0.1%SDS at 50-65 °C, and exposed for autoradiography at -80 °C. For semiquantative RT-PCR, first strand cDNAs were synthesized using SuperScript 2 (Life Technologies) with random primer and 1 mg of Poly(A)+ RNAs or 3-g 3µg of total RNAs described above. Primer sequences were 5'-ID NO: 35), 3'-(SEQ GACCAAAGCCGAGCGACTGCGGC 1, 5'-(SEQ ID NO: 36) for Las-TCGAAGAAGTAGTTCTGTGGC TGACATCCGTAAAGACCTCTATGCC (SEQ ID NO: 37), 3, -AAG CAC TTG CGG TGCACG ATG GAG (SEQ ID NO: 38) for b-actin. All reactions involved initial denaturation at 94 °C for 3 min followed by 30-35 cycles at 94 °C for 30 sec. 55 °C for 30sec, 72 °C for 30 sec (for Las1), and 21 cycles at 94 °C for 30 sec, 68 °C for 30sec, 72 °C for 30 sec (for -actin) (for β-actin) on PTC- 100 Programmable Thermal Controller (MJ Research).